

Translation

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 0000054239		FOR FURTHER ACTION	See Form PCT/IPEA/416
International application No. PCT/EP2004/000237	International filing date (day/month/year) 15.01.2004	Priority date (day/month/year) 22.01.2003	
International Patent Classification (IPC) or national classification and IPC C07D 333/22			
Applicant BASF AKTIENGESELLSCHAFT			

<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>5</u> sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> (sent to the applicant and to the International Bureau) a total of _____ sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>																									
<p>4. This report contains indications relating to the following items:</p> <table><tr><td><input checked="" type="checkbox"/></td><td>Box No. I</td><td>Basis of the report</td></tr><tr><td><input type="checkbox"/></td><td>Box No. II</td><td>Priority</td></tr><tr><td><input type="checkbox"/></td><td>Box No. III</td><td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td></tr><tr><td><input type="checkbox"/></td><td>Box No. IV</td><td>Lack of unity of invention</td></tr><tr><td><input checked="" type="checkbox"/></td><td>Box No. V</td><td>Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td></tr><tr><td><input checked="" type="checkbox"/></td><td>Box No. VI</td><td>Certain documents cited</td></tr><tr><td><input type="checkbox"/></td><td>Box No. VII</td><td>Certain defects in the international application</td></tr><tr><td><input type="checkbox"/></td><td>Box No. VIII</td><td>Certain observations on the international application</td></tr></table>		<input checked="" type="checkbox"/>	Box No. I	Basis of the report	<input type="checkbox"/>	Box No. II	Priority	<input type="checkbox"/>	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability	<input type="checkbox"/>	Box No. IV	Lack of unity of invention	<input checked="" type="checkbox"/>	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement	<input checked="" type="checkbox"/>	Box No. VI	Certain documents cited	<input type="checkbox"/>	Box No. VII	Certain defects in the international application	<input type="checkbox"/>	Box No. VIII	Certain observations on the international application
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Date of submission of the demand	Date of completion of this report																								
Name and mailing address of the IPEA/	Authorized officer																								
Facsimile No.	Telephone No.																								

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/EP2004/000237

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language _____, which is the language of a translation furnished for the purposes of:
- ☐ international search (Rule 12.3 and 23.1(b))
- ☐ publication of the international application (Rule 12.4)
- ☐ international preliminary examination (Rule 55.2 and/or 55.3)
2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:
- ☐ the international application as originally filed/furnished
- ☒ the description:
- pages 1-4 _____ as originally filed/furnished
- pages* _____ received by this Authority on _____
- pages* _____ received by this Authority on _____
- ☒ the claims:
- nos. 1-8 _____ as originally filed/furnished
- nos.* _____ as amended (together with any statement) under Article 19
- nos.* _____ received by this Authority on _____
- nos.* _____ received by this Authority on _____
- ☒ the drawings:
- sheets 1/1 _____ as originally filed/furnished
- sheets* _____ received by this Authority on _____
- sheets* _____ received by this Authority on _____
- ☐ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.
3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages _____
- ☐ the claims, nos. _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing (*specify*): _____
- ☐ any table(s) related to sequence listing (*specify*): _____
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages _____
- ☐ the claims, nos. _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing (*specify*): _____
- ☐ any table(s) related to sequence listing (*specify*): _____

* If item 4 applies, some or all of those sheets may be marked "superseded."

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

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Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-8	YES
	Claims		NO
Inventive step (IS)	Claims	1-8	YES
	Claims		NO
Industrial applicability (IA)	Claims	1-8	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

1. Subject matter of the independent claims

The application relates to 3-methylamino-1-(2-thienyl)-1-propanone and acid addition salts thereof (independent claim 1) and to the use of these compounds (independent claim 3) as intermediates in the preparation of duloxetine, and also to a corresponding method (independent claim 6).

Note: Product claim 2 has been drafted as an independent claim. This is presumably a mistake, and it should be drafted as dependent on claim 1.

2. Prior art documents

Reference is made to the following documents (the reference numbers will be retained throughout the remainder of the procedure):

- D1: WO 2004/020391 A (MERCK PATENT GMBH; NIESERT CLAUS-PETER (DE); FABIAN KAI (DE); KRALIK), 11 March 2004
- D2: EP-A-0 457 559 (LILLY CO ELI), 21 November 1991
- D3: LIU H et al.: "CHEMO-ENZYMATIC SYNTHESIS OF THE ANTIDEPRESSANT DULOXETINE AND ITS ENANTIOMER", CHIRALITY, WILEY-LISS, NEW YORK, US, Vol. 12, No. 1, 2000, pages 26-29

Box No. V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

With regard to document D1, see Box VI below. D1 will be disregarded in the comments which follow.

3. Novelty (PCT Article 33(2)) and inventive step (PCT Article 33(3))

The compounds claimed in claims 1 and 2 are novel over documents D2 and D3 and the other prior art documents covered by the provisions of PCT Rule 64.1(b). The same applies to the use and process claims (claims 3 to 8), which relate to the use of these compounds as intermediates in the preparation of duloxetine.

Claims 1 to 8 are inventive because the processes known from the closest prior art according to D2 and D3 involve different synthesis routes. In the prior art the alcohol function is always formed first by reduction of the corresponding carbonyl precursor, before the introduction of the monomethyl amino group. The technical problem of interest, namely that of providing an alternative process for preparing duloxetine, is thus solved in a non-obvious and inventive way.

4. Industrial applicability (PCT Article 33(4))

Claims 1 to 8 in the present application are industrially applicable (PCT Article 33(4)).

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Box No. VI

Certain documents cited

1. Certain published documents (Rule 70.10)

Application No.
Patent No.Publication date
(day/month/year)Filing date
(day/month/year)Priority date (valid claim)
(day/month/year)

The compounds claimed in claims 1 and 2 are anticipated by document D1, even though D1 is not regarded as prior art under PCT Rule 64.1(b). The validity of the priority claim has not been checked.

2. Non-written disclosures (Rule 70.9)

Kind of non-written disclosure

Date of non-written disclosure
(day/month/year)Date of written disclosure
referring to non-written disclosure
(day/month/year)

See supplemental
sheet